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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/757,708 01/14/2004 Derek O' Hagan PP-19768.002 3852

27476 7590 01/04/2007
NOVARTIS VACCINES AND DIAGNOSTICS INC.
CORPORATE INTELLECTUAL PROPERTY R338
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EXAMINER

POPA, ILEANA

ART UNIT	PAPER NUMBER
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1633

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS 01/04/2007 PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/757,708

Applicant(s)

O' HAGAN ET AL.

Examiner

Ileana Popa

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 October 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28, 31-39, 42-48, 52-64, 6, and 72-89 is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 5, 6, 8-10, 12, 13, 15-18, 23, 26-28, 31, 34-39, 42, 44-48, 52-55, 61, 69, 76-79 and 86 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

Continuation of Disposition of Claims: Claims withdrawn from consideration are 4,7,11,14,19-22,24,25,32,33,43,56-60,62-64,72-75,80-85 and 87-89.

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

2. Claims 29, 30, 40, 41, 49-51, and 65-68 have been cancelled. Claims 4, 7, 11, 14, 19-22, 24, 25, 32, 33, 43, 56-60, 62-64, 72-75, 80-85, and 87-89 have been withdrawn. Claims 1 and 38 have been amended. No new matter was introduced by these amendments.

Claims 1-3, 5, 6, 8-10, 12, 13, 15-18, 23, 26-28, 31, 34-39, 42, 44-48, 52-55, 61, 69, 76-79, and 86 are under examination.

Response to Arguments

Double Patenting

3. Claims 1-3, 5, 6, 9, 10, 12, 13, 15-18, 23, 26, 28-31, 34-42, 44-48, 50, 52-55, 61, 69, 76-79, and 86 remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5-19, 24-26, and 35-40 of the U.S. Patent No. 6,884,435 for the reasons of record set forth in the prior action. Applicants' arguments filed on 10/02/2006 have been fully considered but they are not persuasive.

Applicant traversed the instant rejection on the grounds that the limitations of the adsorbed first polynucleotide constituting at least 5% of the total weight of the

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microparticle and of the microparticle comprising 0.5 to 2 wt% cationic surfactant are not taught or suggested by the claims of the patent. Applicant submits that the patent specification can be used as a dictionary to learn the meaning of a term, but the disclosure may not be used as prior art in an obviousness-type double patenting rejection (MPEP 804). Applicant argues that, even if the specification could be used in the instant rejection, the general passages cited in the Office action (column 13, lines 10-39, column 14, lines 6-10) do not render the claims obvious because the passages pertain generally to macromolecules and there is no disclosure that the ranges (i.e., macromolecule to microparticle and detergent to polymer ratios) are applicable in their entirety to each and every species embraced by the broad genus of macromolecules. Applicant argues that Example 7 of the patent showing achieved loads of 0.8-2.36% (i.e., less than the claimed 5%) for 1-4% input plasmid proves their point. Applicant continues arguing that Tables 3 and 4 of the instant specification disclose the surprising result that microparticle with moderate amounts of cationic detergent and high polynucleotide loadings like those claimed were found to exhibit enhanced immunogenicity as compared to naked DNA and microparticle having higher amount of cationic detergent. For the reasons above, Applicant requests the withdrawal of the rejection.

Contrary to Applicant's assertions, the patent specification was only used to define the microparticles and not as prior art. The microparticles are defined as having a macromolecule to microparticle ratio in the range of 0.1 to 5% and comprising 0.5 to 1% cationic surfactant, range that anticipates the claimed 0.5 to 2% and therefore, one

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of skill in the art would know that these ranges could be applied to any macromolecule of interest because the patent teaches this. Nowhere in the disclosure is any indication that particular macromolecules are excluded. Moreover, the patent claims are specifically drawn to polynucleotides, therefore it would be very clear to one of skill in the art that these ranges are applicable to polynucleotides. The results presented in Example 7 do not prove that a loading of 5% cannot be achieved. Example 7 shows that loading efficiency is not 100% and therefore, in order to achieve a desired loading of 5% , one would have to use more than 5% input polynucleotide. The results clearly demonstrate that broad loading ranges can be obtained and that higher loadings can be achieved by using increasing amounts of input polynucleotide (see Table 4). With respect to the argument that microparticles with moderate amounts of cationic detergent and high polynucleotide loadings were unexpectedly found to have enhanced immunogenicity, it is noted that the claims do not particularly claim this combination, they are drawn to microparticles comprising a wide range of cationic surfactant amounts. These particles were only compared to naked DNA and to microparticles having higher amounts of cationic surfactant and, although it is clear that they are superior to the above, the results do not demonstrate that they are superior to other microparticles. It is routine in the art to vary the relative ratios of the microparticle components and test for the combinations that result in better activity. However, identifying the optimal ratios is not equal to unexpected superior activity, which requires comparison to other microparticles besides the ones claimed by the instant invention. The results only identify the optimal ratios to be used, but do not say anything about

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their performance as compared to other microparticles disclosed in the art and therefore an unexpected enhanced immunogenicity was not demonstrated. Moreover, the '435 patent teaches particles identical to the ones claimed by the instant invention and it is not clear why identical microparticles would have different activities.

For the reasons above the rejection is maintained.

4. Claims 1-3, 5, 6, 9, 10, 12, 13, 15-18, 23, 26, 28-31, 34-37, 52-55, 61, 69, 76-79, and 86 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 8, 10, 11, 13, 15-21, 24-27, 30, and 31 of the U.S. Application No. 11/113,861 for the reasons of record set forth in the prior action. Applicants' arguments filed on 10/02/2006 have been fully considered but they are not persuasive.

Applicants traversed the instant rejection on the same grounds as above, because Application No. 11/113,861 is a continuation of Application No. 09/581,772, which matured as the U.S. Patent No. 6,884,435 and therefore, the arguments set forth above are applicable to the provisional double patenting as well.

The rejection is maintained for the reasons stated above.

35 USC § 112/101

5. The rejection of claim 50 under 35 U.S.C. § 112/101 as being indefinite/not being a proper process claim is withdrawn because Applicant cancelled the claim on...

35 USC § 112, enablement

6. The rejection of claims 40, 41, and 50 under 35 U.S.C. § 112 as not meeting the enablement requirement is withdrawn because Applicant cancelled the claims on 10/02/2006.

7. The rejection of claims 39, 42, and 44-48 under 35 U.S.C. § 112 as not meeting the enablement requirement is withdrawn in response to Applicants arguments filed on 10/02/2006.

8. The rejection of claim 38 under 35 U.S.C. § 112 as not meeting the enablement requirement is withdrawn in response to Applicants amendment filed on 10/02/2006.

35 USC § 102

9. Claims 1-3, 5, 6, 9, 10, 12, 13, 15-18, 23, 26, 28-31, 34-42, 44-48, 50, 52-55, 61, 69, 76-79, and 86 remain rejected under 35 U.S.C. § 102(e) as being anticipated by O'Hagan et al. (U.S. Patent No. 6,884,435) for the reason of record set forth in the prior Office action. Applicants' arguments filed on 10/02/2006 have been fully considered but they are not persuasive.

Applicant traversed the instant rejection on the grounds that O'Hagan et al. do not teach or suggest microparticles in which an adsorbed polynucleotide-containing species constitute at least 5% of the total weight of the microparticles and in which the microparticles comprise 0.5 to 2 wt% cationic surfactant. Applicant argues that

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microparticle with moderate amounts of cationic detergent and high polynucleotide loadings like those claimed were unexpectedly found to exhibit enhanced immunogenicity as compared to naked DNA and microparticle having higher amount of cationic detergent. For the reasons above, Applicant requests the withdrawal of the rejection.

Contrary to Applicant's assertions, O'Hagan et al. teach all the limitation of the instant claims (see above). With respect to the argument of an unexpected enhanced immunogenicity see also above.

35 USC § 103(a)

10. Claims 1-3, 5, 6, 8-10, 12, 13, 15-18, 27-31, 34-39, 42, 44-48, 52-55, 61, and 69 remain rejected under 35 U.S.C. § 103(a) as being unpatentable over Singh et al. (Proc Natl Acad Sci USA, 2000, 97: 811-816) for the reason of record set forth in the prior Office action. Applicants' arguments filed on 10/02/2006 have been fully considered but they are not persuasive.

Applicant traversed the instant rejection on the grounds that Singh et al. do not teach or suggest microparticles with 5% adsorbed polynucleotides and 0.5 to 2 wt% cationic surfactant. With respect to the claimed ranges, Applicant disagrees that it would have been obvious to one of skill in the art to vary the parameters with the purpose of optimizing. Applicant argues that microparticles with moderate amounts of cationic surfactant and high polynucleotide loadings were unexpectedly found to have enhanced immunogenicity, not only relative to naked DNA, but also relative to

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microparticles having higher amounts of cationic surfactants. Applicant continues arguing that a particular parameter must first be recognized as a result-effective variable before it can be argued that it is obvious to optimize the parameter, and that the Examiner did not present any evidence that the claimed parameters are so recognized. Therefore, Applicants requests the withdrawal of the rejection.

Contrary to Applicant's assertions, although Singh et al. do not teach the claimed ranges, it would have been obvious to one of skill in the art to vary these parameters with the purpose of optimizing the results. The prior art recognizes that microparticle performance is a function of loading, composition, and ratio between different components and for this reason it is routine in the art to vary these parameters and select the combination that results in better activity (see for example Singh et al. for loading optimization, p. 813, Table 2, p. 814, Fig. 2). With respect to the argument of unexpected enhanced immunogenicity, since the claimed microparticles were not compared with the microparticles of Singh et al., Applicant cannot claim superior activity. Applicant can only claim that the instant microparticle comprising moderate amounts of cationic surfactant are better than the instant particles comprising higher amounts of cationic surfactant (see also above).

11. Claims 1-3, 5, 6, 8-10, 12, 13, 15-18, 23, 27-31, 34-39, 42, 44-48, 52-55, 61, 69, and 76-79 remain rejected under 35 U.S.C. § 103(a) as being unpatentable over Singh et al. (Proc Natl Acad Sci USA, 2000, 97: 811-816), as applied to claims 1-3, 5, 6, 8-10, 12, 13, 15-18, 27-31, 34-39, 42, 44-48, 52-55, 61, and 69, in view of Thalhammer et al.

(Endocrine Regulations, 2001, 35: 143-166) and Diwan et al. (Journal of Controlled Release, 2002, 85: 247-262) for the reason of record set forth in the prior Office action. Applicants' arguments filed on 10/02/2006 have been fully considered but they are not persuasive.

Applicant traversed the instant rejection of the grounds that Thalhammer et al. and Diwan et al. do not remedy the deficiencies of Singh et al. Applicant argues that, while Thalhammer et al. and Diwan et al. may teach CpG adjuvants, they do not teach adsorbing them to microparticles as claimed. Therefore, Applicant requests the withdrawal of the rejection.

Contrary to Applicants assertions, although Thalhammer et al. and Diwan et al. do not specifically teach adsorbing the CpG to the microparticles, they do teach the use of CpG in combination with DNA vaccines. Moreover, Diwan et al. teach that the co-delivery of CpG and antigen in nanoparticles is a more efficient means of immunization as compared to the use of the delivery of antigen in nanoparticles and CpG in solution (p. 254, column 2).

Conclusion

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not

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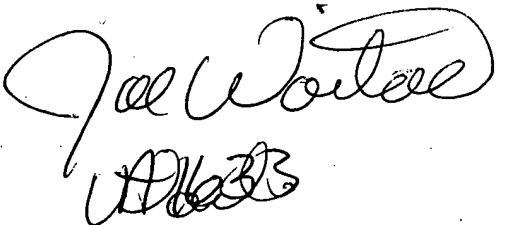
mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ileana Popa whose telephone number is 571-272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ileana Popa, PhD



Joe Woitach
UP 1633